

## AMENDMENTS TO THE CLAIMS:

Claims 1-3, 5, 10-13, 19, 20, 34-36, 40-46, 48-55, 108, 109, 113, 114-116, 118-120 and 122-126 are pending. Please cancel claims 6, 7, 9, 14, 16, 18, 56, 57, 72-75, 91, 127-129 and 137 without prejudice or disclaimer. Please amend claims 1, 5, 12, 13, 18, 43, 108, 113, 115 and 122 as set forth below. This listing of claims replaces all prior versions and listings of claims in the application.

## LISTING OF CLAIMS:

1. (Currently amended) ~~A An isolated, substantially purified single-chain polypeptide, comprising a membrane-type serine protease (MTSP) portion that is a protease domain of a type-II membrane-type serine protease (MTSP) or a catalytically active fragment thereof, portion of an MTSP protease domain, wherein:~~

~~the MTSP portion protease domain or catalytically active fragment thereof is the only portion of the single-chain polypeptide from the MTSP; and~~

~~the MTSP portion protease domain or catalytically active fragment thereof has serine protease activity.~~

2. (Previously presented) The substantially purified polypeptide of claim 1, wherein the MTSP is not expressed on endothelial cells.

3. (Original) The substantially purified polypeptide of claim 1, wherein the MTSP is not expressed on normal endothelial cells *in vivo*.

4. (Cancelled).

5. (Currently amended) The substantially purified polypeptide of claim 1 that consists ~~essentially~~ of the protease domain of an MTSP or a catalytically active portion of the protease domain.

6. - 9. (Cancelled).

10. (Withdrawn) The substantially purified polypeptide of claim 1, wherein the MTSP portion has an N-terminus that comprises IVNG, ILGG, VGLL or ILGG.

11. (Previously Presented) The substantially purified polypeptide of claim 1, wherein the MTSP is selected from among MTSP1, MTSP3, MTSP4 and MTSP6.

12. (Currently amended) The substantially purified polypeptide of claim 1, wherein the MTSP portion protease domain ~~has~~ is a sequence of amino acids ~~acid residues~~ ~~selected from the group consisting of the sequences~~ set forth as amino acids 615-855 of SEQ ID No. 2, as amino acids ~~acid residues~~ 205-437 of SEQ ID NO. 4, as the amino acids ~~acid residues~~ in SEQ ID No. 6 [[,]]-and- or as amino acids 217-443 in SEQ ID No. 12.

13. (Currently amended) The substantially purified polypeptide of claim 1 that has at least about 40%, 60%, 80%, 90% or 95% sequence identity with a protease domain that ~~comprises the whose~~ sequence of amino acids ~~acid residues~~ is set forth as amino acids ~~acid residues~~ 615-855 of SEQ ID No. 2, as amino acids ~~acid residues~~ 205-437 of SEQ ID NO. 4, as the amino acids ~~acid residues~~ in SEQ ID No. 6, or as amino acids ~~acid residues~~ 217-443 in SEQ ID No. 12.

Claims 14 - 18 (Cancelled).

19. (Previously presented) The polypeptide of claim 1, wherein a free Cys in the protease domain is replaced with another amino acid, whereby the resulting polypeptide exhibits proteolytic activity.

20. (Previously presented) The polypeptide of claim 1, wherein a free Cys in the protease domain is replaced with a serine.

Claims 21- 33 (Cancelled).

34. (Previously presented) The polypeptide of claim 1, wherein the MTSP is selected from among corin, MTSP1, enteropeptidase, human airway trypsin-like protease (HAT), TMPRSS2, and TMPRSS4.

35. (Previously presented) A conjugate, comprising:

a) a polypeptide of claim 1, and  
b) a targeting agent linked to the protein directly or via a linker, wherein the conjugate has serine protease activity.

36. (Original) The conjugate of claim 35, wherein the targeting agent permits  
i) affinity isolation or purification of the conjugate;  
ii) attachment of the conjugate to a surface;  
iii) detection of the conjugate; or  
iv) targeted delivery to a selected tissue or cell.

Claims 37 – 39 (Cancelled)

40. (Previously presented) A solid support comprising two or more polypeptides of claim 1 linked thereto either directly or via a linker.

41. (Previously presented) The support of claim 40, wherein the polypeptides comprise an array.

42. (Previously presented) The support of claim 41, wherein the array comprises polypeptides having different MTSP protease domains.

43. (Withdrawn) A method for identifying candidate anti-tumor compounds that modulate inhibit the protease activity of an MTSP, comprising:  
contacting a polypeptide of claim 1 with a substrate proteolytically cleaved by the MTSP, and, either simultaneously, before or after, adding a test compound or plurality thereof; measuring the amount of substrate cleaved in the presence of the test compound; and selecting compounds that change the amount cleaved compared to a control, whereby compounds that modulate the activity of the MTSP are identified.

44. (Withdrawn) The method of claim 43, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

45. (Withdrawn) The method of claim 43, wherein a plurality of the test compounds are screened simultaneously.

46. (Withdrawn) The method of claim 43, wherein the change in the amount cleaved is assessed by comparing the amount cleaved in the presence of the test compound with the amount in the absence of the test compound.

47. (Cancelled)

48. (Withdrawn) The method of claim 43, wherein a plurality of the polypeptides are linked to a solid support, either directly or via a linker.

49. (Withdrawn) The method of claim 43, wherein the polypeptides comprise an array.

50. (Withdrawn) The method of claim 43, wherein the polypeptides comprise a plurality of different MTSP proteases.

51. (Withdrawn) A method of identifying a compound that specifically binds to a single chain protease domain of an MTSP, comprising:

contacting a polypeptide of claim 1 with a test compound or plurality thereof under conditions conducive to binding thereof; and

identifying compounds that specifically bind to the MTSP single chain protease domain or compounds that inhibit binding of a compound known to bind to the MTSP single chain protease domain, wherein the known compound is contacted with the polypeptide before, simultaneously with or after the test compound.

52. (Withdrawn) The method of claims 51, wherein the polypeptide is linked either directly or indirectly via a linker to a solid support.

53. (Withdrawn) The method of claim 51, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

54. (Withdrawn) The method of claim 51, wherein a plurality of the test substances are screened for simultaneously.

55. (Withdrawn) The method of claim 52, wherein a plurality of the polypeptides are linked to a solid support.

56. -107. (Cancelled).

108. (Currently Amended) A conjugate, comprising:

- a) an MTSP3 or an MTSP4 or the MTSP6 of claim 91 12; and
- b) a targeting agent linked to the protein directly or via a linker.

109. (Previously presented) The conjugate of claim 108, wherein the targeting agent permits

- i) affinity isolation or purification of the conjugate;
- ii) attachment of the conjugate to a surface;
- iii) detection of the conjugate; or
- iv) targeted delivery to a selected tissue or cell.

Claims 110 – 112 (Cancelled).

113. (Currently Amended) A solid support comprising two or more ~~MTSP3 polypeptides and/or MTSP4 polypeptides and/or the MTSP6 polypeptides of claim 90~~ 12 linked thereto either directly or via a linker

114. (Previously presented) The support of claim 113, wherein the polypeptides comprise an array.

115. (Withdrawn) A method for identifying compounds that modulate the protease activity of an MTSP of claim 1, -selected from an MTSP3 or an MTSP4 or the MTSP6 of claim 91, comprising:

contacting the MTSP of claim 1 with a substrate proteolytically cleaved by the MTSP, and, either simultaneously, before or after, adding a test compound or plurality thereof; measuring the amount of substrate cleaved in the presence of the test compound; and selecting compounds that change the amount cleaved compared to a control, whereby compounds that modulate the activity of the MTSP are identified.

116. (Withdrawn) The method of claim 115, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

117. (Cancelled).

118. (Withdrawn) The method of claim 115, wherein the change in the amount cleaved is assessed by comparing the amount cleaved in the presence of the test compound with the amount in the absence of the test compound.

119. (Withdrawn) The method of claim 115, wherein a plurality of the test substances are screened for simultaneously.

120. (Withdrawn) The method of claim 119, wherein a plurality of the polypeptides are linked to a solid support.

121. (Cancelled).

122. (Withdrawn) A method of identifying a compound that specifically binds to an MTSP protease domain selected from an MTSP3, an MTSP4 and the MTSP6 of claim 91, comprising:

contacting the an MTSP polypeptide protease domain of claim 12 with a test compound or plurality thereof under conditions conducive to binding thereof; and

identifying compounds that specifically bind to the MTSP.

123. (Withdrawn) The method of claim 122, wherein the polypeptide is linked either directly or indirectly via a linker to a solid support.

124. (Withdrawn) The method of claim 122, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

125. (Withdrawn) The method of claim 122, wherein a plurality of the test substances are screened for simultaneously.

126. (Withdrawn) The method of claim 125, wherein a plurality of the polypeptides are linked to a solid support.

Claims 127 – 137 (Cancelled).